BUDAPEST UNIVERSITY OF TECHNOLOGY AND ECONOMICS

DOCTORAL THESIS BOOKLET

Complex Methods for Automated X-ray Image Analysis

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November 11, 2017

Abstract

X-ray imaging based diagnosis plays an important role in today's clinical practice. It is essential for the detection, localization and analysis of disorders and diseases, contributing to an effective treatment. One of the most important usages is the visualization of early stage cancerous tumors, useful for targeted screening of the population.

In the current work, novel methods are proposed for computer assisted analysis of X-ray images. Solutions in this area already exist; however, with limited precision and scope. The goals of the proposed new methods are threefold. First, to improve the precision of automated diagnosis to make it more dependable and reduce misdiagnosis. Second, to extend the scope of findings to enable a more comprehensive usage. Third, to enable automated diagnosis on new modalities promising better accuracy to cost ratio.

The contributions of this thesis can be categorized into three major areas. The first group of proposed methods contains improved and novel image filters for lesion detection aiming at a more precise and broader set of findings in projection images. Proposals include a shape constrained extension of a gradient convergence based filter, also a contrast based method suitable for handling background variations, and a learning filter based on outlier detection.

The second group of proposals include methods combining heterogeneous information sources for improving X-ray scan analysis. First, an algorithm is described for the optimal combination of different object detectors for a common figure of merit. Second, the effect of bone shadow removal is investigated on chest radiographs and a method is given for improving lesion detection. Third, new kernel functions are proposed to improve classification accuracy of lesions. As a part of this, an optimal set of image features are selected for a kernel in feature space, other kernels directly comparing images are borrowed from different image recognition tasks, and novel features are investigated based on patient metadata and external diagnostic systems.

Results in the third group aim at the analysis of digital tomosynthesis scans, a relatively new and unexplored modality

of X-ray based chest imaging. First, a common vascular tree segmentation method is modified and extended to adapt well for the new modality. Second, several existing and newly proposed lesion detector filters are compared based on their utility for digital tomosynthesis.

As an application of the previous results, complete computer aided detection schemes ares proposed for lung lesions both for chest radiographs and digital tomosynthesis scans. The two modalities are compared.

1 Introduction

Medical imaging plays a critical role in the clinical practice of today, helping diagnostics tasks of human and machine experts. When the subject of a study is the internals of living organisms, medical imaging most often relies on radiodensity scans made by using X-rays. The most well known such modalities are X-ray computed tomography (CT) and conventional radiography, commonly called X-ray. In addition, digital tomosynthesis (DTS) is a new, emerging technique aiming to fill the gap between CT and radiography.

The goal of X-ray imaging is to visualize the inner structure of the human body. This is done by approximating the radiodensity of regions in space. As different organs tend to have different radiodensity, various types of tissues become distinguishable. The initial form of X-ray imaging, used in radiography, is only able to measure the aggregated radiodensity along the straight lines determined by the path of the X-rays. The application of the results of Radon, 1917 is one way to enable the approximation of radiodensity of distinct points in space from multiple projections, making three-dimensional visualization also possible.

Tomosynthesis is one such technique reconstructing a three-dimensional volume of the subject. It started to evolve along the works of Plantes, 1932; Garrison et al., 1969; Miller, MoCurry, and Hruska, 1971; Grant, 1972. While the basic theory of reconstruction is shared with CT, the resulting scans are fundamentally different. The angular range of projections in tomosynthesis is limited, resulting in moderate resolution along the depth axis (perpendicular to the detector plane); however, every projection yields a full, two-dimensional radiograph with high resolution. The state-of-the-art version of tomosynthesis relies on digital image acquisition to improve the precision and flexibility of reconstruction, and it is called digital tomosynthesis.

In its current state, X-ray imaging is able to reliably solve several problems in clinical practice. For example, radiography clearly shows bone fractures, while CT can visualize small tumors in various organs. Radiography can help to detect a vast number of lung diseases like pneumonia or emphysema.

In the current study, the focus is on the lung and a subset of its diseases with highest importance: lung cancer, tuberculosis and a more general group of interstitial lung diseases. These can be characterized as the following.

Lung cancer is one of the most common causes of cancer death. Incidence is high and survival rate is extremely low. According to recent statistics from the US the number of expected new cases for 2014 involve 0.07% of the population, and 5 years survival rate is only around 18%, see Siegel et al., 2014. One of the main reasons behind low survival rates is the fact that most cures are only effective in the early and symptomless stage of the disease when it often stays undetected. It has been shown by Kramer et al., 2011 that mortality can be reduced with an early diagnosis when done in a mostly symptomless stage of the disease. Therefore the success rate of the treatment can potentially be increased by improving the accuracy of diagnoses and with regular examination of the population (i.e. screening). Achieving either one poses great challenges.

Tuberculosis (TB) – a type of interstitial lung disease (ILD) – is another serious disease of today with high incidence and fatality rate. It mostly affects the developing world, and Human Immunodeficiency Virus (HIV) infected patients are particularly at risk. The estimated number of new cases in 2012 were roughly 0.12% of the global population while 0.02% of all death cases are accounted to TB, see World Health Organization et al., 2013. The current treatments for TB are effective, provided that the patient is diagnosed early enough. This is often not the case in the developing world due to the lack of resources.

2 Selected challenges of X-ray based diagnostics

Despite its strong capabilities, at least three main problems can be identified with current X-ray based methods, undermining precise diagnosis.

First, X-ray is a kind of ionizing radiation, posing a health risk for the patient. Health risks are low but not negligible according to Brenner et al., 2001 and Sodickson et al., 2009, so lowering dosage is still desirable. Changing dosage means a trade-off between health risks and image quality, and the latter is directly affecting the diagnostic value of the examination. Keeping the diagnostic value high while lowering dosage is possible either by improved hardware, by more sophisticated image processing or by more careful analysis of the images. Computer aided detection (CADe) – the addition of a machine expert to the clinical practice – contributes to the solution by facilitating more careful analysis.

Another problem of current X-ray techniques is the high cost of operation. The time needed for creating a scan per patient combined with high device costs and the time needed to analyze the resulting images all contribute to major costs, especially as image detail level increases. On the other hand, at least annual examination of a large part of the population would be necessary to enable early diagnosis of the diseases discussed above, confirmed by studies of Shlomi et al., 2014 and Furlow, 2014. This would result in unacceptable costs with current technology. By helping human analysts in their work by providing an automated analysis by a CADe system, the overall cost can be considerably reduced.

The third problem of X-ray based diagnostics is frequent misdiagnosis caused by the difficulty of correct interpretation of the scans. The difficulty mainly originates from the following properties. First, there is a vast number of anatomical structures present in chest images, and they overlap in many areas in a scan. Second, there is no color information to distinguish different tissues, just a single channel, intensity, and the contrast is typically very low. Intensity is not even calibrated except for CT, and low dose techniques – like chest radiography (CXR) – are particularly affected. Lastly, the anatomical structures in question are varying in shape and hard to model. All these difficulties make correct diagnosis hard even for highly trained professionals. As a result, there is a tendency to overlook subtle signs of diseases, typically small cancerous tumors. It has been shown that more than 30% of early stage tumors are overlooked in chest radiographs in clinical practice, see studies of Muhm et al., 1983, Quekel et al., 1999, Shah et al., 2003 and Doi, 2007. This can be mitigated by more careful analysis of the images, for example by adding a CADe system as an extra automated observer.

Involving a computer aided detection system in the clinical process has the potential to mitigate all three problems, confirmed multiple studies, for example Kobayashi et al., 1996; MacMahon, Engelmann, et al., 1999; De Boo et al., 2009. Even partially solving these issues can have a large positive impact on the population, therefore these problems serve as the main motivation for conducting research in the area of automated X-ray analysis.

3 Selected open problems for computer aided detection in X-ray images

In the past decades, automatic lung lesion detection for chest radiography (CXR) and CT has been extensively studied. A few of the most important examples are the works of Chen, Suzuki, and MacMahon, 2011; Snoeren et al., 2010; Hardie et al., 2008; Campadelli, Casiraghi, and Artioli, 2006; A.M.R. Schilham, Van Ginneken, and Loog, 2006; Coppini et al., 2003; Wei et al., 2002.

Most proposed methods follow a common scheme. A model is assumed describing the targeted objects, and image processing algorithms are applied to enhance nodule shadows based on this model. The models are designed to include all the possible variations of the targeted lesions to minimize the number of false negative cases. The imperfection of the models implies that many false positive regions are also enhanced. After extracting the enhanced, lesion-model-like areas, false findings are partly eliminated with the help of a classifier. The input of the classifier consists of various features that can help to distinguish true and false positive findings.

Although a tremendous amount of work has been invested in previous solutions, they have not reached a comfortable level of accuracy and still fall behind human experts. They suffer from a high number of false positive and false negative cases, for example common working points of CADe systems produce 2-5 false positive findings per image. False positives make human examiners abandon their correct diagnosis in favor of the false findings of CADe (see B. de Hoop et al., 2010), and at the same time examiners might lose trust in the system when they observe a false negative case. Additionally, more time is needed for the analysis with CADe (see De Boo et al., 2009), especially when there are many false findings. This justifies new attempts to contribute alternative methods for the improvement of results. In the following, I identify common problems of the existing approaches, and set the path for my own research.

Most of the solutions start with a lesion-enhancing filter assuming a perfectly circular lesion model. This is true for typical blob detectors like the Laplacian of Gaussian, difference of Gaussians and different specializations of the convergence index filters from Kobatake and Hashimoto, 1999. Such filters distinguish non-circular objects less and often unable to find elongated or irregular lesions. A potential room for improvement is to generalize the filters to adapt better to non-perfect circular shapes. In my study, I modified the shape constraints of convergence index filters to improve their selectivity to non-perfect circular shapes.

Most algorithms are optimized for finding small lesions with diameter less than 30 mm. Some experts argue that detecting larger lesions have little diagnostic utility as it is already too late to start treatment in this stage. This is not always the case: according to a lung tumor staging method reported by Mountain, 1997, patients with tumors larger than 30 mm still have an approximately 57% five-year survival rate as opposed to patients with early stage tumors with 67% five-year survival rate. Extending the scope towards such lesions is a potential solution, but larger scale imposes different challenges, for example more frequent overlap with background structures and a different intensity characteristic of lesions. One goal of my research was to develop a filter that is less sensitive to background variations and has a response optimized for larger lesions.

Another problem is the narrow focus on lung nodules. This narrow scope may be inadequate for a CADe at screening as lung nodules are only one possible manifestation of lung cancer. Others with less definite shape and boundaries are often called infiltrated areas, a generic term for the sign of increased density or substance abnormal in the lung. According to MacMahon, Doi, et al., 1990, infiltrated areas are by far the most frequent findings on chest radiographs, which remains true even if only subtle, hard-to-detect ones are considered. Furthermore, infiltrated areas can indicate other serious diseases desirable to mark at screening, for example pneumonia, TB or other ILD-s. As most studies in the past focused on small nodules, B. van Ginneken, Hogeweg, and Prokop, 2009 suggested a change of focus, claiming that finding only nodules is not enough to detect signs of mortal diseases. Only a very few earlier attempts were made to detect signs in the lung beyond lung nodules and neither of them attempted to find a broad set of diseases including lung nodules and infiltrated areas with state-of-the-art methods. I aimed at developing a general lesion filter having a reduced dependence on shape and is mostly based on intensity, so it is better suited for finding infiltrated areas.

In terms of the top-level design of detection schemes, one can notice that most authors employ a linear processing scheme where every step consumes the output of a single previous step. This is contrary to the popular principle of ensemble methods, see for example the summary by Zhou, 2012 from the field of machine learning. Applying ensembles is a possible way to address the issue of narrow scope, and at the same time can also improve accuracy. With this assumption, I sought a combination of multiple filters to have a single detector sensitive to both infiltrated areas and lung nodules of any size, while keeping the accuracy superior to any individual filter.

Various forms of noise are present in X-ray scans, like structured anatomical background noise, detector noise or noise due to the scattering of X-rays, and these are all potential sources of false findings for CADe algorithms. Nevertheless, most earlier approaches omit any preprocessing to address this issue. Even the ones that do noise filtering, approach it in a general way and neglect most of the available domain specific knowledge. As radiographs have many common features, like the presence of a similarly structured ribcage, one can try to use these common features for a more targeted noise filtering. As an efficient method to eliminate the shadow of bones was already available, the goal of my study was to measure its effect on lesion detection and to develop image features that can augment lesion classification based on knowledge about the ribcage.

Focusing on the false positive reduction methods, most proposals include a classification step relying on various features and similarity functions of lesion images. New features and similarity functions have the potential of improving classification accuracy and there are several methods missing from previous works for CADe. On the other hand, the number of employed features across different solutions is extremely large, and there is no consensus about the subset of really useful ones. Efficient application of new features make more advanced feature selection methods necessary. I was focusing on improving classification accuracy by proposing new similarity functions, new features and combining them all together in an efficient way.

As opposed to chest radiography, not many previous attempts were made to address the problem of CADe in the field of DTS. This leaves a large set of open problems related to this modality. After analyzing DTS scans and also studying the related field of CT, one can identify lesion enhancement and vascular and bronchial tree detection as two potentially high-impact subproblems. The many existing algorithms from the field of CT and CXR naturally rise the question whether they are useful for DTS scans, and if so, what particular approach yields the best results. I was aiming to answer some of the open questions by creating, adapting, applying and comparing multiple lesion enhancer and vascular tree segmenter methods to DTS scans.

It is also unanswered whether CADe can perform better on DTS scans than radiographs, and if so, how large is the difference. The lack of published results on publicly available scan sets prevented answering these questions before. By combining the best results from my studies, my goal was to answer by a fair comparison between CADe methods for CXR and DTS.

4 Summary of new scientific results

4.1 Filter algorithms for the enhancement of lesions in projection images

The first contribution introduces individual filter algorithms for object recognition focusing on X-ray image analysis. The research was motivated by two main goals. The first is to supersede existing algorithms for problems arising in X-ray image analysis. The other is to provide suitable building blocks for ensemble systems introduced in Contributions 2 and 3, enabling a wider scope of findings.

Contribution 1 *I developed novel filter algorithms for analyzing X-ray scans and demonstrated their superior accuracy compared to former methods in specific subproblems of lesion detection.*

1.1 Convergence index filters *I developed the constrained sliding band filter (CSBF) for enhancement of round objects, a generalization of existing convergence index filters. Compared to existing methods, the new formulation enables more control over the target shape to enhance precision and depends on gradient vectors to be more robust against structured noise. I experimentally proved that the new filter is superior to other convergence index filters in recognizing deformed shapes and also in finding lung lesions in X-ray applications. At the same time, I proved algorithmic complexity* *to be the same as the baseline. The new filter has been published first in G. Orbán, Á. Horváth, and G. Horváth, 2010.*

1.2 Blob detection on object boundaries *I developed a blob filter algorithm that can utilize background segmentation information to reduce sensitivity for structured noise. For this purpose, I developed a modified local contrast enhancement filter taking into account background segmentation and combined it with a matched filter. To adapt the method for X-ray analysis I proposed a matching template optimal for the problem and a location restriction step based on simple lung modeling. I demonstrated that the new method is applicable in multiple domains of X-ray analysis and outperforms a baseline method. The new filter has been published first in G. Orbán and G. Horváth, 2012a.*

1.3 Outlier detection for lesion recognition *I developed a filter for outlier detection in images based on local intensity distribution estimation. I complemented the method with a lightweight image registration algorithm to make it applicable for X-ray analysis. To improve the robustness of registration, I defined a coordinate system tied to lung segmentation results. I demonstrated that the new filter is applicable for infiltrated area detection in chest radiographs. The method has been published first in G. Orbán and G. Horváth, 2012b.*

Background The first part of Contribution 1 generalizes convergence index filters, a family of filters targeted at spherical objects and mainly relying on gradient vector direction. The main idea behind convergence index filters was originally described by Kobatake and Hashimoto, 1999, while they were refined and applied for X-ray image analysis problems several times later, for example by Pereira, Mendonça, and Campilho, 2007. Accuracy of current filters is not optimal when the target shape is different from a perfect sphere or the noise is structured. My contribution improves on the most advanced member of the filter family in the following way. First, it makes the filter better suited for problems where the target shape can vary from a perfect circle by introducing a new shape constraint. Second, it reduces sensitivity to background structures by adding a gradient magnitude dependent term.

Earlier works of Burgess, X. Li, and Abbey, 1997 and Samei, Flynn, and Eyler, 1999 concluded that in general, structured noise is a more serious problem than wide-spectrum or random noise for radiograph analysis. The second part of my contribution addresses a special case where the source of noise is a known background structure. I borrowed ideas from template matching and local contrast enhancement described by Lee, 1980 to solve this problem. The main benefit of the method is handling the targeted special cases, therefore complementing other filters to widen overall scope of CADe.

The third part of this contribution is involved with another special case of object recognition, where the shape of the target object is unknown, but the background follows similar patterns between cases. This problem arises when extending the scope of radiography CADe to infiltrated areas. The solution borrows the general idea of outlier detection from the field of statistics. To make the method applicable, a fast approximation of image registration was necessary. I solved this problem by incorporating domain specific knowledge in the form of lung segmentation information. The new method demonstrates the utility of the outlier detection framework in a different field, while it also gives a natural solution for the special object detection problem.

4.2 Fusion of heterogeneous information to improve lesion detection

The paradigm of ensemble methods has been getting more attention lately. For many complex problems, instead of searching for the single best solution, the general approach is shifting towards the creation and combination of many solutions for the same problem. When a proper combination method is used, the ensemble system can outperform every single solution.

A vast number of examples can be found in the research literature for both methods and applications. A collection of the basic techniques can be found in Zhou, 2012, but the principle goes beyond the field of machine learning. Successful applications include the ensemble outperforming all other solutions for the Automatic Nodule Detection 2009 challenge (ANODE09), see Bram van Ginneken et al., 2010.

The main focus of Contribution 2 is on new ways to apply ensembles for X-ray analysis. While Contributions 2.1 and 2.2 combine together image filters, Contribution 2.3 is involved with ensembles for lesion classification.

Contribution 2 *I proposed new ways to combine methods to improve the accuracy of X-ray image analysis. I demonstrated that using ensembles provides accuracy gains in the domain of X-ray based diagnosis both when applied at the level of image filter algorithms and at the level of kernel functions for classification.*

2.1 Combination of heterogeneous object filters *I introduced a scheme for the combination of different object detectors and proposed a method for merging their results. I proved that the merging method is optimal when the area under the free-response receiver operating curve is used as the figure of merit. I applied the new method for lesion detection in chest radiographs and digital tomosynthesis, and experimentally proved that the new method improves accuracy compared to the individual detectors and a baseline combination. The initial idea has been published in G. Orbán and G. Horváth, 2012b.*

2.2 Suppression of background structures *I proved by measurements that bone shadow removal improves the accuracy of automated lesion detection in chest radiographs. I developed new classification features and demonstrated on a large sample that they help the elimination of falsely detected structures caused by bone shadows. The results has been published in*

Áron Horváth et al., 2013, while a preliminary version appeared in Simkó et al., 2009.

2.3 Kernel functions for lesion classification *I developed new kernel functions for lesion classification. First, I combined existing and new image features to build a kernel in image feature space and reduced dimensionality with the help of sparse Bayesian learning. Second, I adapted kernel functions comparing objects directly in image space to X-ray scans. Third, I proposed kernel functions relying on non-local features, in particular patient age and the presence of lung fluid. I demonstrated in X-ray analysis problems that all three methods have discriminative power and combining them can yield further benefits when using a proposed multiple kernel learning framework. The image space kernels and the method of combination have been published in G. G. Orbán and Gábor Horváth, 2017.*

Background The first part of the contribution proposes a novel way of obtaining an ensemble of object recognition methods. The goal is to combine the output of different image filters optimizing the area under the free-response receiver operating characteristic, that is the most common measure in the field of X-ray image analysis, described in Chakraborty and Winter, 1990. While the proposed method is general purpose, the application examples come from the field of X-ray image analysis. The applications for chest radiographs and digital tomosynthesis satisfied two different goals. The former demonstrated that the method is useful for getting a more comprehensive set of findings without increasing the rate of false results. The latter application showed improved accuracy while maintaining the scope of findings.

The second part of the contribution investigates the compensation of disturbing anatomical structures. The difficulty of chest radiograph analysis is mainly a consequence of the presence of a large number of overlapping anatomical structures like shadows of bones. This is one of the main reasons why current CADe systems fail to produce precise detections. The presence of the ribcage and the clavicles in radiographs can cause two common types of detection errors.

They may conceal the shadows of abnormalities by darkening the image thus reducing contrast or just by increasing clutter – like edges, intensity variations – in some areas. This can result in false negative cases. On the other hand, rib crossings on the radiographs tend to mimic convex structures appearing to be real lesions. This can introduce false positive findings. These two phenomena seriously affect both human examiners and CADe systems; however, the hiding effect is problematic mostly for radiologists and physicians while the CADe system suffers rather from false positives due to rib crossings.

Recent studies of Freedman et al., 2011, Soleymanpour, Pourreza, et al., 2011 and F. Li et al., 2011 confirmed that bone shadow suppression can help human examiners in finding lung nodules. The goal of my study was to investigate if there is a similar effect for computer aided lesion detection systems and to propose an efficient scheme for the usage of bone shadow removal. The bone shadow removal system used in this study and published in Áron Horváth et al., 2013 was not my own work.

The last part of the contribution focuses on lesion classification with kernel methods. Kernel methods – e.g. SVM classifiers originally proposed by Cortes and Vapnik, 1995 – are popular for object recognition and image classification tasks. As the success of these methods is fundamentally determined by the expressive power of the underlying kernel function, a great amount of work has been invested in finding suitable kernels for image classification. In this study, three fundamentally different approaches for kernel construction were applied and combined to improve the accuracy of classification.

The most common approach in current CADe systems is to calculate handcrafted features directly from lesion images and to use the resulting feature vector as the input for generic kernel functions. The approach needs features with good separation power; however, a high input dimensionality is often harmful for generalization. I addressed the problem by proposing new features besides the ones used in previous studies and by employing a feature selection algorithm to reduce dimensionality of the input space. The selection method is based on sparse Bayesian learning described in Tipping, 2001 and Wipf and Nagarajan, 2007.

The second approach defines kernels directly in the space of the input images. This approach is common in general object recognition tasks but has hardly been used for lesion classification. The proposed solution is based on kernel descriptors introduced by Bo, Ren, and Fox, 2010. The kernels were adapted to address the challenges of X-ray scans, for example limited color space, overlapping objects, less prominent edges and high resolution.

The third approach was motivated by the radiological screening practice, where the scan itself provides only partial information for the analysis. Expert radiologists also take into account patient metadata, medical history and signs of other diseases. I focused on the applicability of patient age and the presence lung fluid, an independent symptom of lung abnormality, for lesion classification. The lung fluid detector used in this study was not my own work, see Kormányos, 2013.

While all three approaches are useful for classifying lesions, combining them promises the best accuracy. Therefore, I proposed a linear multiple kernel learning scheme. The main strength of the scheme is the ability to handle kernel functions with very different classification power.

The results of feature selection and using patient metadata has not been published so far.

4.3 Computer aided detection for digital tomosynthesis

In this part I focus on problems arising in the field of digital tomosynthesis (DTS). DTS is a promising imaging modality for lung diagnosis as it is able to visualize subtle lung lesions well while operating with lower dosage than CT. On the other hand, not many CADe methods are available for DTS, and unclear if it serves better as a lung screening method than the widespread chest radiography.

While it is already known according to Vikgren et al., 2008 that detection accuracy of human examiners are higher using DTS scans compared to using chest radiographs, this has not been shown for CADe systems before. This part of my thesis proposes new methods hoping to contribute to the answer: I start with investigating subproblems of automated analysis of DTS scans in Contributions 3.1 and 3.2. Then, in Application 2, I combine the methods into a CADe scheme and compare them with a CXR-based CADe system using the same patients.

From the image processing perspective, DTS analysis is a three-dimensional volume processing problem where the task is to enhance or detect objects according to a lesion model. In this sense, many ideas can be borrowed from the much more researched field of CT CADe. On the other hand, the DTS problem has its unique properties. Due to the geometry of image acquisition, depth resolution along the anterior/posterior axis is very limited, while the resolution in the coronal plane is considerably higher than for CT. This effect has to be taken into account when developing the models for recognition algorithms to improve accuracy and reduce complexity.

Contribution 3 *I developed new methods for analyzing digital tomosynthesis scans, focusing on vascular tree segmentation and lesion enhancement filtering. I used the new methods to build a complete lesion detection scheme. I demonstrated on a large sample that the resulting system can achieve superior detection accuracy compared to CXR-based CADe systems.*

3.1 Vascular and bronchial tree segmentation *I developed an adaptation of the Frangi vessel filter tailored for digital tomosynthesis scans. I demonstrated that the proposed method is able to efficiently enhance vessels and bronchi. I experimentally proved that vascular and bronchial tree segmentation can improve accuracy of nodule detector algorithms. Parts of this work has been published in Gergely Orbán and Gábor Horváth, 2014.*

3.2 Comparison of object detector methods *I adapted existing object detectors for the problem of lesion detection in digital tomosynthesis volumes. I developed a new Hessian matrix based filter better suited for the* *domain. I provided a comparison of the above methods on publicly available scans where my proposed method outperformed the other filters. Parts of this work has been published in Gergely Orbán and Gábor Horváth, 2014.*

Background A common property of radiographic chest images is the visibility of the vascular and bronchial structures. These structures, especially when perpendicular to the plane of view, can mimic small nodules, therefore their segmentation is an important aid for nodule detector algorithms to avoid false detections. The presence or absence of these structures in certain regions also carry diagnostic information, making their segmentation useful for CADx also beyond nodule detection.

For the basis of my studies in Contribution 3.1 I have chosen a well known vessel detector described in Frangi, 2001, due to its popularity in other fields of medical imaging. The method turned out to be useful after modifying the formula to handle the strong depth blur typical to DTS scans and adding post-processing steps based on lung segmentation information.

In Contribution 3.2, I focused on lesion detection. The field of DTS CADe, in particular lesion detection is relatively unexplored: only a few methods have been proposed in earlier works, and none of them has been evaluated on public data. As many potentially applicable algorithms exist for similar problems in other domains, there is room for further studies. The main goal of this contribution is to investigate the relative merits of existing and new spherical object detector methods, and to select the most efficient ones for potential application in a comprehensive CADe scheme. I also addressed specific parameter selection problems. Methods involved in the study include the adaptation of the vessel detector by Frangi, 2001, a different second-derivative based filter from Feuerstein et al., 2009, the widespread determinant of Hessian (DoH) blob detector, template matching as proposed in WEI et al., 2010, the CSBF filter proposed earlier in Contribution 1.1 and finally the new Hessian-based detector.

5 Practical applications of the proposed methods

Application 1: A CADe system for lesion detection in CXR The first application builds on the new methods of contributions 1 and 2 to address the problem of lesion detection in chest radiographs. Earlier methods exist, e.g. Chen, Suzuki, and MacMahon, 2011; Snoeren et al., 2010; Hardie et al., 2008; Campadelli, Casiraghi, and Artioli, 2006; A.M.R. Schilham, Van Ginneken, and Loog, 2006; Coppini et al., 2003; Wei et al., 2002; however, detection accuracy of even the best solutions still falls behind of human examiners. My proposed scheme takes one step forward by combining the methods presented in other contributions of my dissertation. I put emphasis on publishing comparable results, partly by relying on the public radiograph database described in Shiraishi et al., 2000 and partly by using multiple acceptance criteria for evaluation. The method has been published in G. Orbán and G. Horváth, 2012b.

The current work resulted in a CADe system integrated into a commercial X-ray system. The development of the X-ray system was a joint effort of the Innomed Medical Developing and Manufacturing Inc, the Pulmonological Clinic of Semmelweis University and the Budapest University of Technology and Economics, supported by the National Development Agency under contract KMOP-1.1.1-07/1-2008-0035. The resulting system is currently in use in multiple lung screening stations across Hungary.

Application 2: A CADe system for lesion detection in DTS In the second application, I developed a computer aided lesion detection scheme for digital tomosynthesis, utilizing novel techniques introduced and discussed in earlier parts of my dissertation. I demonstrated that the resulting CADe scheme based on the modality of digital tomosynthesis can be more accurate than a similar system processing chest radiographs. I did this by comparing detection accuracy of the proposed system and the one described in Application

1. The same set of patients were used for the comparison. The proposed CADe scheme has been published in Gergely Orbán and Gábor Horváth, 2014.

The main goal of the application was to provide building blocks for a DTS scanner still under development. The participants of the development were the Innomed Medical Developing and Manufacturing Inc, the Pulmonological Clinic of Semmelweis University and the Budapest University of Technology and Economics, and the project was partially supported by the National Development Agency under contract KMR-12-1-2012-0122.

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